

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

125261

REMS

Appendix A. REMS Document

BLA 125261 STELARA™ (ustekinumab)

Human interleukin 12 and 23 antagonist

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOALS

To evaluate and mitigate the potential risks of serious infections and malignancy, and reversible posterior leukoencephalopathy syndrome (RPLS) associated with STELARA™ by:

- alerting and warning healthcare providers and patients about the risks
- informing and educating healthcare providers about the Psoriasis Longitudinal Assessment and Registry (PSOLAR) voluntary disease-specific patient registry

II. REMS ELEMENTS

A. MEDICATION GUIDE

In accordance with 21 CFR 208.24, a Medication Guide will be appended to the package insert and will be provided by Centocor Ortho Biotech Inc. and/or its affiliates by either:

1. Providing Medication Guides in sufficient numbers to distributors, packers, or authorized dispensers to permit the authorized dispenser to provide a Medication Guide to each patient receiving a prescription for the drug product; or
2. Providing the means to produce Medication Guides in sufficient numbers to distributors, packers, or authorized dispensers to permit the authorized dispenser to provide a Medication Guide to each patient receiving a prescription for the drug product.

Medication Guides will be included in each single unit carton containing one vial and dispensed in accordance with 21 CFR 208.24.

The Medication Guide will also be available on the STELARA™ patient and professional websites.

Please see appended Medication Guide (Attachment A).

B. COMMUNICATION PLAN

Centocor Ortho Biotech Inc. will implement a communication plan to the following healthcare providers:

- Dermatologists and dermatology healthcare providers (HCPs) who are likely to prescribe and/or inject STELARA™
- Oncologists who may treat malignancies potentially associated with the use of immunosuppressants for chronic inflammatory and autoimmune disease and will need to ascertain cases of malignancy after a long latency period
- Rheumatologists who may co-manage with dermatologists moderate to severe psoriasis patients with psoriatic arthritis
- Infectious disease specialists and gastroenterologists who may be consulted about infections and will need to understand the potential for infectious complications of IL-12/IL-23 blockade
- Neurologists who may treat RPLS

The communication plan will provide for the dissemination of risk information about serious infection, malignancy, and RPLS, and encourage patient participation and physician referral to PSOLAR investigator sites (a voluntary psoriasis registry).

Elements of the communication plan:

1. A Dear Healthcare Professional letter (see Attachment B) will be distributed to dermatologists, oncologists, rheumatologists, infectious disease specialists, gastroenterologists, and neurologists. This will be distributed within 60 days of STELARA™ approval.

A Professional Label and a copy of the Medication Guide will also be distributed in this communication.

2. A Dear Pharmacist letter (see Attachment C) will be distributed to pharmacists. This will be distributed within 60 days of STELARA™ approval.

A Professional Label and a copy of the Medication Guide will also be distributed in this communication.

3. Dissemination of information about serious infection, malignancy, and RPLS to health care providers through certain dermatology, oncology, rheumatology, infectious diseases, and gastroenterology professional societies' journals:

- 1) For display as a panel/poster and distribution as printed material at all dermatology and oncology scientific meetings where the company has a sponsored booth
- 2) For quarterly presentation as a printed information piece in the *Journal of the American Academy of Dermatology* and the *Archives of Dermatology* for 3 years

- 3) For quarterly presentation as a printed information piece in the *Journal of Clinical Oncology* and *Blood* for 5 years
- 4) For twice yearly presentation as a printed information piece in *Arthritis and Rheumatism*, the *Journal of Infectious Disease*, the *American Journal of Gastroenterology*, and *Gastroenterology* for 3 years

The REMS Journal Information Piece is appended to this document (see Attachments D, E, F, G, and H).

4. Centocor Ortho Biotech Inc. will enhance participation in PSOLAR, a voluntary, disease-specific registry (which is comprised of patients receiving systemic therapies including other biologic agents), by outreach to dermatologic societies, inclusion of PSOLAR contact information in communication materials, and proactively educating dermatologists about PSOLAR.

C. TIMETABLE FOR SUBMISSION OF ASSESSMENTS

Centocor Ortho Biotech Inc. will submit REMS Assessments to the FDA according to the table below. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Centocor Ortho Biotech Inc. will submit each assessment so that it will be received by the FDA on or before the due date.

<u>Assessment Submission</u>	<u>Timing Interval Relative to Approval of the REMS</u>	<u>Date of Submission to the FDA (month/year)</u>
1st Assessment	18 months after approval	March, 2011
2nd Assessment	3 years after approval	September, 2012
3rd Assessment	7 years after approval	September, 2016

Attachment A Medication Guide

MEDICATION GUIDE

STELARA™ (stel ar' a)

(ustekinumab)

Injection

Read this Medication Guide before you start taking STELARA™ and each time before you get an injection. There may be new information. This Medication Guide does not take the place of talking with your doctor about your medical condition or treatment with STELARA™.

What is the most important information I should know about STELARA™?

STELARA™ is a medicine that affects your immune system. STELARA™ can increase your chances of having serious side effects, including:

Serious Infections: STELARA™ may lower the ability of your immune system to fight infections and may increase your risk of infections. Some people have serious infections while taking STELARA™, including tuberculosis (TB), and infections caused by bacteria, fungi, or viruses. Some people have to be hospitalized for treatment of their infection.

- Your doctor should check you for TB before starting STELARA™.
- If your doctor feels that you are at risk for TB, you may be treated with medicine for TB before you begin treatment with STELARA™ and during treatment with STELARA™.
- Your doctor should watch you closely for signs and symptoms of TB during treatment with STELARA™.

You should not start taking STELARA™ if you have any kind of infection unless your doctor says it is okay.

Before starting STELARA™, tell your doctor if you think you have an infection or have symptoms of an infection such as:

- fever, sweats, or chills
- muscle aches
- cough
- shortness of breath
- blood in your phlegm
- weight loss

- warm, red, or painful skin or sores on your body
- diarrhea or stomach pain
- burning when you urinate or urinate more often than normal
- feel very tired
- are being treated for an infection
- get a lot of infections or have infections that keep coming back
- have TB, or have been in close contact with someone who has TB.

After starting STELARA™, call your doctor right away if you have any symptoms of an infection (see above).

STELARA™ can make you more likely to get infections or make an infection that you have worse.

People who have a genetic problem where the body does not make any of the proteins interleukin 12 (IL-12) and interleukin 23 (IL-23) are at a higher risk for certain serious infections. These infections can spread throughout the body and cause death. It is not known if people who take STELARA™ will get any of these infections, because of the effects of STELARA™ on these proteins in your body.

Cancers:

STELARA™ may decrease the activity of your immune system and increase your risk for certain types of cancers. Tell your doctor if you have ever had any type of cancer.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS):

RPLS is a rare condition that affects the brain and can cause death. The cause of RPLS is not known. If RPLS is found early and treated, most people recover. Tell your doctor right away if you have any new or worsening medical problems including:

- headache
- seizures
- confusion
- vision problems

What is STELARA™?

STELARA™ is a prescription medicine used to treat adults 18 years and older with moderate or severe psoriasis that involves large areas or many areas of their body, who may benefit from taking injections or pills (systemic therapy) or phototherapy (treatment using ultraviolet light alone or with pills).

STELARA™ may improve your psoriasis but may also lower the ability of your immune system to fight infections. This may also increase your risk for certain types of cancer.

It is not known if STELARA™ is safe and effective in children.

It is not known if taking STELARA™ for more than 2 years is safe and effective.

What should I tell my doctor before receiving STELARA™?

Before receiving STELARA™, tell your doctor if you:

- have any of the conditions or symptoms listed in the section “What is the most important information I should know about STELARA™?”
- have recently received or are scheduled to receive an immunization (vaccine). People who take STELARA™ should not receive live vaccines. Tell your doctor if anyone in your house needs a vaccine. The viruses used in some types of vaccines can spread to people with a weakened immune system, and can cause serious problems. **You should not receive the BCG vaccine during the one year before taking STELARA™ or one year after you stop taking STELARA™.**
- receive phototherapy for your psoriasis.
- have any other medical conditions.
- are pregnant or planning to become pregnant. It is not known if STELARA™ will harm your unborn baby. You and your doctor should decide if you will take STELARA™.
- are breast-feeding or plan to breast-feed. It is thought that STELARA™ passes into your breast milk. You should not breast-feed while taking STELARA™ without first talking with your doctor.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Especially tell your doctor if you take:

- other medicines that affect your immune system.
- certain medicines that can affect how your liver breaks down other medicines.

Ask your doctor or pharmacist if you are not sure if your medicine is one that is listed above.

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How will I receive STELARA™?

- STELARA™ is given by injection under the skin (subcutaneous injection).
- STELARA™ should only be given by a healthcare provider as directed by your doctor.
- Your doctor will decide the right dose of STELARA™ for you and how often you should receive it.

- Be sure to keep all of your scheduled follow-up appointments.

What should I avoid while receiving STELARA™?

You should not receive a live vaccine while taking STELARA™. See “What should I tell my doctor before taking STELARA™?”

What are the possible side effects of STELARA™?

STELARA™ can increase your chances of having serious side effects. See “What is the most important information I should know about STELARA™?”

Common side effects of STELARA™ include:

- upper respiratory infections
- headache
- tiredness

These are not all of the possible side effects of STELARA™. Tell your doctor about any side effect that bothers you or that does not go away. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about STELARA™

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide.

This Medication Guide summarizes the most important information about STELARA™. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about STELARA™ that was written for healthcare professionals. For more information, go to www.STELARAinfo.com or call 1-800-457-6399.

What are the ingredients in STELARA™?

Active ingredient: ustekinumab

Inactive ingredients: sucrose, L-histidine, and polysorbate 80.

Manufactured by Cilag AG,
Schaffhausen, Switzerland
for

Centocor Ortho Biotech Inc.

Horsham, PA 19044

Revised September 2009

This Medication Guide has been approved by the U.S. Food and Drug Administration.

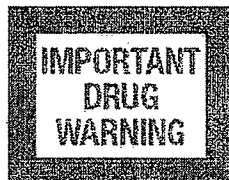
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Attachment B Dear Healthcare Professional Letter



Centocor Ortho Biotech Inc.



Dear Healthcare Professional:

The purpose of this letter is to inform you of important safety information for STELARA™ (ustekinumab), a new human monoclonal antibody which has been approved by the Food and Drug Administration (FDA) for the treatment of adult patients (18 years or older) with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy. STELARA™ targets interleukin-12 (IL-12) and interleukin-23 (IL-23). FDA has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary for STELARA™ to ensure that the benefits of the drug outweigh the potential risks of serious infections and malignancy, and reversible posterior leukoencephalopathy syndrome (RPLS).

IMPORTANT SAFETY INFORMATION FOR POTENTIAL RISKS OF SERIOUS INFECTIONS AND MALIGNANCIES, AND RPLS

The following information is important for healthcare professionals and patients treated with STELARA™:

Infections

- STELARA™ may increase the risk of infections and reactivation of latent infections. Serious bacterial, fungal, and viral infections, some requiring hospitalization, were observed in patients receiving STELARA™. STELARA™ should not be given to patients with a clinically important active infection and should not be administered until the infection resolves or is adequately treated. Instruct patients to seek medical advice if signs or symptoms suggestive of an infection occur. Exercise caution when considering use of STELARA™ in patients with a chronic infection or a history of recurrent infection.

Theoretical Risk for Vulnerability to Particular Infections

- Individuals genetically deficient in IL-12/IL-23 are particularly vulnerable to disseminated infections from mycobacteria, salmonella, and *Bacillus Calmette-Guerin* (BCG) vaccinations. Serious infections and fatal outcomes have been reported in such patients.
- It is not known whether patients with pharmacologic blockade of IL-12/IL-23 from treatment with STELARA™ will be susceptible to these types of infections. Appropriate diagnostic testing should be considered as dictated by clinical circumstances.

Pre-Treatment Evaluation of Tuberculosis (TB)

- Evaluate patients for TB infection prior to initiating treatment with STELARA™. Do not administer STELARA™ to patients with active TB. Initiate treatment of latent TB before administering STELARA™.
- Consider anti-tuberculosis therapy prior to initiation of STELARA™ in patients with a past history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed.
- Patients receiving STELARA™ should be monitored closely for signs and symptoms of active TB during and after treatment.

Malignancies

- STELARA™ (ustekinumab) is an immunosuppressant and may increase the risk of malignancy. Malignancies were reported among subjects who received STELARA™ in clinical studies.

- The safety of STELARA™ has not been evaluated in patients who have a history of malignancy or who have a known malignancy.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS)

- One case of RPLS has been reported in a STELARA™-treated subject.
- RPLS is a neurological disorder, which is not caused by demyelination or a known infectious agent. RPLS can present with headache, seizures, confusion and visual disturbances. It has been associated with preeclampsia, eclampsia, acute hypertension, cytotoxic agents and immunosuppressive therapy.
- If RPLS is suspected, discontinue STELARA™ and administer appropriate treatment.

REPORTING PATIENT ADVERSE EVENTS

It is important that you report all serious adverse events that occur in patients using STELARA™. If you have a patient who develops a serious infection or RPLS while being treated with STELARA™, or if you have a patient with cancer at any time after receiving STELARA™ therapy, it is important that you report the case even if you do not think there is a causal relationship.

The information that you can provide may inform therapy and monitoring decisions for psoriasis patients.

Reporting is easy and maintains patient confidentiality. Your patient's name or contact information is not needed. *HIPAA does not apply* to this adverse event reporting.

You can report your cases to the STELARA™ manufacturer or directly to FDA.

- Centocor Ortho Biotech Inc. at 1-800-457-6399
- MedWatch (FDA safety information and adverse event reporting program) at 1-800-332-1088 or online at www.fda.gov/medwatch/report.htm

VOLUNTARY REGISTRY INFORMATION

PSOLAR (PSOoriasis Longitudinal Assessment and Registry) is a Centocor Ortho Biotech Inc.-sponsored voluntary psoriasis registry that will be available to enroll patients treated with STELARA™. Please call 1-888 PSOLAR-5 or go to www.clinicaltrials.gov for more information.

Please see the enclosed:

- STELARA™ package insert, and
- Medication Guide

Please Note: This letter does not include a comprehensive description of the serious and significant risks associated with the use of STELARA™. Please read the accompanying Full Prescribing Information and Medication Guide for a complete description of the serious and significant risk that may be associated with the use of STELARA™. You are advised to discuss the risks that may be associated with STELARA™ therapy with patients and their caregivers. We have enclosed a copy of the STELARA™ Medication Guide, which is required to be provided to patients with every filled prescription. This Medication Guide contains information that can be used to facilitate discussions about the potential risks of therapy.

Sincerely,



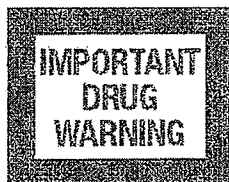
Peter Callegari, MD
Vice President, Medical Affairs

Enclosures

Attachment C Dear Pharmacist Letter



Centocor Ortho Biotech Inc.



Dear Pharmacist:

The purpose of this letter is to inform you of important safety information for STELARA™ (ustekinumab), a new human monoclonal antibody which has been approved by the Food and Drug Administration (FDA) for the treatment of adult patients (18 years or older) with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy. STELARA™ targets interleukin-12 (IL-12) and interleukin-23 (IL-23). FDA has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary for STELARA™ to ensure that the benefits of the drug outweigh the potential risks of serious infections and malignancy, and reversible posterior leukoencephalopathy syndrome (RPLS).

FDA requires that a copy of the enclosed STELARA™ Medication Guide be distributed to each patient (or agent such as a caregiver) who fills a prescription for STELARA™. A copy of the STELARA™ Medication Guide will be packaged with every vial of STELARA™.

Should you require additional copies of the STELARA™ Medication Guide, you may

- Request copies from Centocor Ortho Biotech Inc. by calling the toll-free medical information line at 1-800-457-6399
- Print copies of the Medication Guide from the STELARA™ website www.stelarainfo.com
- Request copies from your drug supplier
- Photocopy the enclosed Medication Guide, after confirming that it is the most current version
- Call the toll-free medical information line at the number above

IMPORTANT SAFETY INFORMATION FOR POTENTIAL RISKS OF SERIOUS INFECTIONS AND MALIGNANCIES, AND RPLS

Important Safety Information is listed in the Warnings and Precautions sections of the Prescribing Information for STELARA™ and Medication Guide for patients.

Infections

- STELARA™ may increase the risk of infections and reactivation of latent infections. Serious bacterial, fungal, and viral infections, some requiring hospitalization, were observed in patients receiving STELARA™. STELARA™ should not be given to patients with a clinically important active infection and should not be administered until the infection resolves or is adequately treated. Instruct patients to seek medical advice if signs or symptoms suggestive of an infection occur. Exercise caution when considering use of STELARA™ in patients with a chronic infection or a history of recurrent infection.

Theoretical Risk for Vulnerability to Particular Infections

- Individuals genetically deficient in IL-12/IL-23 are particularly vulnerable to disseminated infections from mycobacteria, salmonella, and *Bacillus Calmette-Guerin* (BCG) vaccinations. Serious infections and fatal outcomes have been reported in such patients.
- It is not known whether patients with pharmacologic blockade of IL-12/IL-23 from treatment with STELARA™ (ustekinumab) will be susceptible to these types of infections. Appropriate diagnostic testing should be considered as dictated by clinical circumstances.

Pre-Treatment Evaluation of Tuberculosis (TB)

- Evaluate patients for TB infection prior to initiating treatment with STELARA™. Do not administer STELARA™ to patients with active TB. Initiate treatment of latent TB before administering STELARA™.
- Consider anti-tuberculosis therapy prior to initiation of STELARA™ in patients with a past history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed.
- Patients receiving STELARA™ should be monitored closely for signs and symptoms of active TB during and after treatment.

Malignancies

- STELARA™ is an immunosuppressant and may increase the risk of malignancy. Malignancies were reported among subjects who received STELARA™ in clinical studies.
- The safety of STELARA™ has not been evaluated in patients who have a history of malignancy or who have a known malignancy.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS)

- One case of RPLS has been reported in a STELARA™-treated subject.
- RPLS is a neurological disorder, which is not caused by demyelination or a known infectious agent. RPLS can present with headache, seizures, confusion and visual disturbances. It has been associated with preeclampsia, eclampsia, acute hypertension, cytotoxic agents and immunosuppressive therapy.
- If RPLS is suspected, discontinue STELARA™ and administer appropriate treatment.

REPORTING PATIENT ADVERSE EVENTS

It is important that you report all serious adverse events that occur in patients using STELARA™. If you are aware of a patient who develops a serious infection or RPLS while being treated with STELARA™, or if you are aware of a patient with cancer at any time after receiving STELARA™ therapy, it is important that you report the case even if you do not think there is a causal relationship. The information that you can provide may inform therapy and monitoring decisions.

Reporting is easy and maintains patient confidentiality. The patient's name or contact information is not needed. *HIPAA does not apply to this adverse event reporting.*

You can report cases to the STELARA™ manufacturer or directly to FDA.

- Centocor Ortho Biotech Inc. at 1-800-457-6399
- MedWatch (FDA safety information and adverse event reporting program) at 1-800-332-1088 or online at www.fda.gov/medwatch/report.htm

Please Note: This letter does not include a comprehensive description of the serious and significant risks that may be associated with the use of STELARA™. Please read the accompanying Full Prescribing Information and Medication Guide for a complete description of the serious and significant risk that may be associated with the use of STELARA™.

Sincerely,



Peter Callegari, MD
Vice President, Medical Affairs

Enclosures

Attachment D Journal Information Piece for Dermatologists

Important Information for Dermatologists about the Potential Risks of Serious Infections and Malignancy, and RPLS with STELARA™ for Psoriasis Therapy

STELARA™ (ustekinumab) is a new human monoclonal antibody that is indicated for the treatment of adult patients (18 years or older) with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

STELARA™ targets interleukin-12 (IL-12) and interleukin-23 (IL-23). Based on data from rodent models and humans genetically deficient for components of IL-12 and IL-23 pathways, there is a theoretical concern that **blockade of IL-12 and IL-23 may increase the risk for serious infections, including mycobacterial and recurrent salmonella infections**. In addition, data from rodent models suggest there is a theoretical concern that **blockade of IL-12 and IL-23 may increase the risk for malignancies**.

One case of Reversible Posterior Leukoencephalopathy Syndrome (RPLS) has been reported in a STELARA™-treated patient in clinical trials. RPLS is a neurological disorder which is not caused by demyelination or a known infectious agent, and can present with headache, seizures, confusion and visual disturbances.

If you have a patient that develops a serious infection or RPLS while being treated with STELARA™, or if you have a patient with cancer at any time after receiving STELARA™ therapy, it is important that you report the case even if you do not think there is a causal relationship.

The information that you, as a STELARA™ prescribing dermatologist, can provide may inform therapy and monitoring decisions for psoriasis patients.

Reporting is easy and maintains patient confidentiality. Your patient's name or contact information is not needed. *HIPAA does not apply* to this adverse event reporting.

You can report your cases to the STELARA™ manufacturer or directly to FDA.

- Centocor Ortho Biotech Inc. at 1-800-457-6399
- MedWatch (FDA safety information and adverse event reporting program) at 1-800-332-1088 or online at www.fda.gov/medwatch/report.htm

PSOLAR (Psoriasis Longitudinal Assessment and Registry): is a **voluntary, disease-specific registry**, developed by Centocor Ortho Biotech Inc., that collects information from psoriasis patients and their treating physicians. Since this registry will continue for 10 years, it will help us better understand the risk of long-latency serious events, such as malignancies, that can occur after exposure to a product such as STELARA™.

For more information on PSOLAR and how to include patients in this voluntary registry, call 1-888-PSOLAR5 (1-888-776-5275) or access www.clinicaltrials.gov and search for PSOLAR.



Attachment E Journal Information Piece for Oncologists

Important Information for Oncologists About Potential Malignancy Risk With STELARA™ for Psoriasis Therapy

STELARA™ (ustekinumab) is a new human monoclonal antibody that is indicated for the treatment of adult patients (18 years or older) with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

STELARA™ targets interleukin-12 (IL-12) and interleukin-23 (IL-23). Based on data from rodent models, there is a theoretical concern that **blockade of IL-12 and IL-23 may increase the risk for malignancies.**

If you are consulted to see a patient with cancer at any time after receiving STELARA™ therapy, it is important that you report the case even if you do not think there is a causal relationship.

The information that you, as an oncologist, can provide may inform therapy and monitoring decisions for psoriasis patients.

Reporting is easy and maintains patient confidentiality. Your patient's name or contact information is not needed. *HIPAA does not apply* to this adverse event reporting.

You can report your cases to the STELARA™ manufacturer or directly to FDA.

- Centocor Ortho Biotech Inc. at 1-800-457-6399
- MedWatch (FDA safety information and adverse event reporting program) at 1-800-332-1088 or online at www.fda.gov/medwatch/report.htm

Attachment F Journal Information Piece for Rheumatologists

Important Information for Rheumatologists about the Potential Risks of Serious Infections and Malignancy, and RPLS with STELARA™ for Psoriasis Therapy

STELARA™ (ustekinumab) is a new human monoclonal antibody that is indicated for the treatment of adult patients (18 years or older) with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

STELARA™ targets interleukin-12 (IL-12) and interleukin-23 (IL-23). Based on data from rodent models and humans genetically deficient for components of IL-12 and IL-23 pathways, there is a theoretical concern that **blockade of IL-12 and IL-23 may increase the risk for serious infections, including mycobacterial and recurrent salmonella infections**. In addition, data from rodent models suggest there is a theoretical concern that **blockade of IL-12 and IL-23 may increase the risk for malignancies**.

One case of Reversible Posterior Leukoencephalopathy Syndrome (RPLS) has been reported in a STELARA™-treated patient in clinical trials. RPLS is a neurological disorder which is not caused by demyelination or a known infectious agent, and can present with headache, seizures, confusion and visual disturbances.

If you have a patient that develops a serious infection or RPLS while being treated with STELARA™, or if you have a patient with cancer at any time after receiving STELARA™ therapy, it is important that you report the case even if you do not think there is a causal relationship.

The information that you, as a rheumatologist that may co-manage patients receiving STELARA™ therapy, can provide may inform therapy and monitoring decisions for psoriasis patients.

Reporting is easy and maintains patient confidentiality. Your patient's name or contact information is not needed. *HIPAA does not apply to this adverse event reporting.*

You can report your cases to the STELARA™ manufacturer or directly to FDA.

- Centocor Ortho Biotech Inc. at 1-800-457-6399
- MedWatch (FDA safety information and adverse event reporting program) at 1-800-332-1088 or online at www.fda.gov/medwatch/report.htm

Attachment G Journal Information Piece for Infectious Disease Specialists

Important Information for Infectious Disease Specialists About Potential Serious Infection Risk With STELARA™ for Psoriasis Therapy

STELARA™ (ustekinumab) is a new human monoclonal antibody that is indicated for the treatment of adult patients (18 years or older) with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

STELARA™ targets interleukin-12 (IL-12) and interleukin-23 (IL-23). Based on data from rodent models and humans genetically deficient for components of IL-12 and IL-23 pathways, there is a theoretical concern that **blockade of IL-12 and IL-23 may increase the risk for serious infections, including mycobacterial and recurrent salmonella infections.**

If you are consulted to see a patient that develops a serious infection while being treated with STELARA™, it is important that you report the case even if you do not think there is a causal relationship.

The information that you, as an infectious disease specialist, can provide may inform therapy and monitoring decisions for psoriasis patients.

Reporting is easy and maintains patient confidentiality. Your patient's name or contact information is not needed. *HIPAA does not apply* to this adverse event reporting.

You can report your cases to the STELARA™ manufacturer or directly to FDA.

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Attachment H Journal Information Piece for Gastroenterologists

Important Information for Gastroenterologists About Potential Serious Infection Risk With STELARA™ for Psoriasis Therapy

STELARA™ (ustekinumab) is a new human monoclonal antibody that is indicated for the treatment of adult patients (18 years or older) with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

STELARA™ targets interleukin-12 (IL-12) and interleukin-23 (IL-23). Based on data from rodent models and humans genetically deficient for components of IL-12 and IL-23 pathways, there is a theoretical concern that **blockade of IL-12 and IL-23 may increase the risk for serious infections, including mycobacterial and recurrent salmonella infections.**

If you are consulted to see a patient that develops a serious infection while being treated with STELARA™, it is important that you report the case even if you do not think there is a causal relationship.

The information that you, as a gastroenterologist, can provide may inform therapy and monitoring decisions for psoriasis patients.

Reporting is easy and maintains patient confidentiality. Your patient's name or contact information is not needed. *HIPAA does not apply* to this adverse event reporting.

You can report your cases to the STELARA™ manufacturer or directly to FDA.

- Centocor Ortho Biotech Inc. at 1-800-457-6399
- MedWatch (FDA safety information and adverse event reporting program) at 1-800-332-1088 or online at www.fda.gov/medwatch/report.htm